UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,954	10/07/2005	Jane Barclay	PN/4-32436A	3004

75074 7590 05/29/2008

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
400 TECHNOLOGY SQUARE
CAMBRIDGE, MA 02139

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,954	BARCLAY ET AL.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-21,23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *4,5,7,9-21,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,8 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2,4-21,23,25 and 26* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, claims 1-3, 6, 8, and 23, in the reply filed on 19 March 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 4-5, 7, 9-21, and 25-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 19 March 2008.

2. The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

3. The response filed on 19 March 2008 has been entered in full. Claim 1 has been amended, claim 3 has been cancelled, and claims 4-5, 7, 9-21, and 25-26 have been withdrawn. Therefore, claims 1-2, 4-21, 23, and 25-26 are pending, and claims 1-2, 6, 8, and 23 are the subject of this Office action.

Information Disclosure Statement

4. The Information Disclosure Statement (IDS) submitted on 04 October 2005 has been considered by the Examiner.

Specification

5. The disclosure is objected to because of the following informalities:

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

7. The use of the trademarks has been noted throughout the Specification. See for example GENBANK™ (pg 9), RNAIMAGE™ (pg 40), LIPOFECTIN™ (pg 45), and TAQMAN™ (pg 46). Trademarks should be capitalized wherever they appear and should be accompanied by the generic terminology. Applicant is encouraged to review and make appropriate corrections to the specification regarding the misuse of trademarks. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

8. The attempt to incorporate essential subject matter into this application by reference to GENBANK™ # AAF75553 and AAA91780 is ineffective because accession numbers can change, and the sequence associated with a particular accession number can change. Since the claimed subject matter relies upon the sequences contained therein and are required for searching the claimed subject matter, Applicant is required to provide a sequence identifier (i.e., SEQ ID NO:#) that corresponds to each accession number. In addition, said submission must comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, Applicant is required to provide (1) a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, (2) a substitute paper copy of that "Sequence Listing", (3) an amendment directing the entry of that paper into the specification, and (4) a statement that the content of the paper and

computer readable copies are the same, and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 through 1.825. The claims and/or instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (i.e., SEQ ID NO: #) be made in the specification and claims wherever a reference is made to that sequence (See M.P.E.P. 2422.04).

Claim Rejections - 35 USC § 112, 1st Paragraph (Enablement)

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 6, 8, and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method to treat or ameliorate chronic pain comprising administering to a subject in need thereof an effective amount of a Mob-5 modulator, wherein the Mob-5 refers to a rat Mob-5 protein according to SEQ ID NO:6 or GENBANK™ # AAF75553 or the human orthologs of Mob-5 (interleukin-24) according to GENBANK™ # AAA91780, does not reasonably provide enablement for a method to treat or ameliorate chronic pain comprising administering to a subject in need thereof an effective amount of a Mob-5 modulator, wherein the Mob-5 refers to all possible variants of Mob-5 that are encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

11. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

12. The claims are drawn quite broadly to a method to treat or ameliorate chronic pain comprising administering to a subject in need thereof an effective amount of a Mob-5 modulator or a pharmaceutical composition comprising an effective amount of a Mob-5 modulator, wherein said Mob-5 modulator inhibits the activity of Mob-5 in said subject. The claims also recite wherein the Mob-5 modulator comprises one or more antibodies to Mob-5, and administering a monoclonal antibody which specifically binds an epitope of Mob-5. While the specification provides adequate guidance for the skilled artisan to make and use inhibitors of Mob-5 wherein the Mob-5 refers to a rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780, it does not provide adequate guidance for a commensurate number of the claimed variants of Mob-5, which the specification teaches can be any and all forms of these polypeptides, including, but not limited to variants, partial forms, isoforms, precursor forms, or fragments of any of the above, from human or any other species (See pg 9).

13. While the Specification teaches that Mob-5 mRNA is upregulated in rat dorsal root ganglia (DRG) in a number of chronic pain models (See 41), and that administering an inhibitor of Mob-5 results in decreased mechanical hyperalgesia (See pg 50), the specification fails to describe other variants of Mob-5 which are either upregulated in chronic pain models, or could be inhibited to exhibit the same effects, and it would require undue experimentation to determine such. Moreover, there is nothing in the instant specification nor the art of record which would lead one skilled in the art to expect, with any level of predictability, that a compound that which the activity of any variant of Mob-5 would have a similar function in the treatment of chronic pain, given the very broad scope of the claims which encompass variants of Mob-5 that do not require any degree of structural or functional similarity to Mob-5. Furthermore, while the Specification provides adequate direction and guidance on how to make and use inhibitors of Mob-5, the specification fails to describe inhibitors of variants of Mob-5, and it would require undue experimentation to determine such. As the specification does not teach how to make and use a number of species that would be commensurate in scope with the claims, it would require undue experimentation by the skilled artisan to practice the invention in a manner commensurate in scope with the claims, given the absence of working examples, the lack of direction and guidance in the specification, the unpredictability in the art, and the very broad scope of the claims.

14. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively

conservative substitutions or no substitutions. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions, and modifications), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, that may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2).

15. Other than the Mob-5 proteins discussed *supra* (i.e., rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780), the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. Based on the very limited number of disclosed species of Mob-5, it is not at all predictable what essential structural features are required for a compound to have the claimed property of being a target for chronic pain, and it would require undue experimentation to determine such. As the specification does not teach how to make and use a number of species that would be commensurate in scope with the claims, it would require undue experimentation for one skilled in the art to practice the invention in a manner commensurate in scope with the claims, given the lack of guidance in the specification and the very broad scope of the claims.

16. Due to the large quantity of experimentation necessary to generate the infinite number of agents that are inhibitors/antagonists of "Mob-5" activity encompassed by the claims; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide binding/activity of the antagonist of "Mob-5"; and the breadth of the claims which fail to recite any structural limitations of "Mob-5"; it would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to make and/or use the Applicants' invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

17. Claims 1-2, 6, 8, and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

18. The claims are drawn quite broadly to a method to treat or ameliorate chronic pain comprising administering to a subject in need thereof an effective amount of a Mob-5 modulator or a pharmaceutical composition comprising an effective amount of a Mob-5 modulator, wherein said Mob-5 modulator inhibits the activity of Mob-5 in said subject. The claims also recite wherein the Mob-5 modulator comprises one or more antibodies to Mob-5, and administering a monoclonal antibody which specifically binds an epitope of Mob-5. While the specification provides adequate written description of Mob-5 and Mob-5 inhibitors, wherein the Mob-5 refers to a rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780, it does not provide adequate written description for a commensurate number of the claimed variants of Mob-5, which the specification teaches can be any and all forms of these polypeptides, including, but not limited to variants, partial forms, isoforms, precursor forms, or fragments of any of the above, from human or any other species (See pg 9), nor does it provide adequate written description for inhibitors of variants of Mob-5.

19. To provide adequate written description and evidence of possession of a claimed genus,

the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of the recitation of "Mob-5", or a desired functional property in the form of the recitation of being an inhibitor/antagonist of "Mob-5" activity. However, there does not appear to be an adequate written description in the specification as filed of any essential structural feature common to molecules that are "Mob-5" or inhibitors/antagonists antagonists of "Mob-5". While the specification provides adequate written description for antibodies which bind a Mob-5 protein, wherein the Mob-5 refers to a rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780, it does not provide adequate written description for a commensurate number of the claimed variants of Mob-5, which the specification teaches can be any and all forms of these polypeptides, including, but not limited to variants, partial forms, isoforms, precursor forms, or fragments of any of the above, from human or any other species (See pg 9), nor does it provide adequate written description for inhibitors of variants of Mob-5. The only adequately described species are the antibodies which bind a Mob-5 protein, wherein the Mob-5 refers to a rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780. Accordingly, the specification does not provide adequate written description of the claimed genus.

20. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey

with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

21. With the exception of the Mob-5 antibodies referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed Mob-5 proteins or the inhibitors/antagonists thereof, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The product itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

22. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

23. Therefore, only antibodies which bind a Mob-5 protein, wherein the Mob-5 refers to a rat Mob-5 protein set forth in SEQ ID NO:6 or GENBANK™ # AAF75553 or the human ortholog of Mob-5 (interleukin-24) set forth in GENBANK™ # AAA91780, but not the full breadth of the claims, meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is

reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, 2nd Paragraph

24. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

25. Claims 1-2, 6, 8, and 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

26. Claims 1, 6, 8, and 23 are rejected as being indefinite for reciting the limitation "Mob-5". The discussion of Mob-5 at pg 9 of the Specification is exemplary rather than limiting, fails to breathe life and meaning into the claim and thus is insufficient to render the claim definite. Since the limitation "Mob-5" encompasses terms such as variants, partial forms, and precursor forms, for which neither the art nor the specification provides an unambiguous definition for, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

27. Claim 6 is rejected as being indefinite because without knowing whether the limitation "or fragments thereof" refers to the antibody or to Mob-5, the metes and bounds of the claim cannot be determined.

28. Claim 23 is rejected as being indefinite because without knowing whether the limitation "or a biologically active fragment thereof" refers to the monoclonal antibody or to an epitope of Mob-5, the metes and bounds of the claim cannot be determined.

29. Claim 2 is rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

30. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

31. Claims 1-2, 6, 8, and 23 is rejected under 35 U.S.C. 102(e) as being anticipated by Liang (U.S. Patent No. 6,902,930, priority to 29 August 2001; previously cited).

32. Liang teaches a method for treating cancer comprising administering a Mob-5 inhibitor (See column 17, lines 4-16, for example). Liang also teaches that the Mob-5 inhibitor can be a polyclonal or monoclonal antibody, or fragments thereof, that either bind to Mob-5 or a Mob-5 receptor (See col. 12, lines 49-59; col. 17, line 27 through col. 18, line 17) and inhibits (i.e., antagonizes) the activity of Mob-5. It is noted that the instant specification discloses cancer pain as the most common type of chronic pain, having both inflammatory and neuropathic components (See pg 3, lines 1-2). Therefore, although Liang is silent with regard to the Mob-5 inhibitor treating or ameliorating chronic pain or chronic neuropathic pain, it is noted that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971)).

Thus, in the absence of evidence to the contrary, the Mob-5 inhibitor administered in the method for the treatment of cancer as taught by Liang would inherently treat or ameliorate the chronic pain or chronic neuropathic pain in the cancer subject. Thus, claims 1-2, 6, 8, and 23 are anticipated by Liang.

Summary

33. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon M. Lockard, Ph.D.
May 21, 2008

/Jon M Lockard/
Examiner, Art Unit 1647